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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/689,281	10/11/2000	Stephen C. Cosenza	6056-277	1158

23973 7590 11/05/2002

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EXAMINER

BAHAR, MOJDEH

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 11/05/2002 16

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/689,281

Applicant(s)

CONSENZA ET AL.

Examiner

Mojdeh Bahar

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period of Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 09 August 2002.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-7 and 12-22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 12-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/09/02 has been entered.

Claims 1-7 and 12-22 are herein examined on the merits in so far as they read on the elected specie and the styryl sulfone compound, E-4-fluorostyryl 4-chlorobenzyl sulfone.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-87 and 12-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reddy et al. WO 99/18608 and Griggs (Embase Abstract AN 1998287056).

Reddy et al. WO 99/18608 teaches a compound of general formula I and II and III (encompassing both E and Z configurations) employed in a method of treating breast and prostate tumor cells, and induce apoptosis of such tumor cells while sparing normal cells, see claims 1-9 and abstract.

Reddy et al. WO 99/18608 does not teach a method comprising the administration of compound of general formula I and II and III (encompassing both E and Z configurations) prior to the administration of mitotic phase cell cycle inhibitor or topoisomerase inhibitor.

Griggs (Embase Abstract AN 1998287056) teaches that cytoprotective agents reduce treatment-related toxicity of anticancer therapy. Griggs specifically teaches the employment of cytoprotective agents with paclitaxel, see abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ anticancer paclitaxel along with a cytoprotective agent such as the styryl sulfone compounds of Reddy et al.

One of ordinary skill in the art would have been motivated to employ anticancer paclitaxel along with a cytoprotective agent such as the styryl sulfone compounds of Reddy et al. because both compounds are known to be effective in treating cancer. It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be useful for the very same purpose, *In re Kerkhoven*, 205 USPQ 1069, 1072 (CCPA 1980). Further, the optimization of regimens is within the purview of the skilled artisan.

The elected specie 4-carboxystyryl-4-chlorobenzylsulfone is allowable over prior art. Therefore the methods of both claim 1 and 18, employing the elected specie, 4-carboxystyryl-4-chlorobenzylsulfone is not seen to be taught or fairly suggested by the prior art.

#### ***Response to Arguments***

Applicant's arguments filed 08/09/02 have been fully considered but they are not persuasive. Applicant first argues that sparing normal cells while inducing apoptosis in tumor

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cells does not mean that the drug is protecting the normal cells because “one of ordinary skill in the art would not consider the absence of a particular drug effect in a cell to indicate a positive interaction between the drug and a cell.” Note that the essence of this invention is the treatment of cancer. More particularly the claims herein set forth a method of lowering the incidence of side effects of anti-neoplastic agents in a patient by employing a “cytoprotective agent.” Reddy teaches that its aryl sulfones are effective anti-tumor agents, yet they “spare” normal cells. The sparing of the normal cells means that the incidence of side effects (on normal cells) is reduced if not eliminated. Therefore Reddy does indeed teach the employment of aryl sulfones as cytoprotective agents. Assuming *arguendo* that Reddy does not teach the cytoprotective qualities of aryl sulfones, at the very least Reddy teaches that styryl sulfone compounds are known to be effective in treating cancer. Topoisomerase inhibitors and mitotic phase cell cycle inhibitors are also well known in treating cancer. It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be useful for the very same purpose, *In re Kerkhoven*, 205 USPQ 1069, 1072 (CCPA 1980).

Applicant further argues that Griggs does not mention aryl sulfone compounds and that aryl sulfones and amifostine (the cytoprotective agent taught in Griggs) have dissimilar chemical structures. Applicant argues that amifostine and aryl sulfones have a “potentially dissimilar pharmacology”. Note that amifostine, is functionally analogous to the aryl sulfones of Reddy since they are both cytoprotective agents.

Applicant further argues that the *Kerkhoven* rejection in the previous office action is not pertinent since the claims are not directed to a composition comprising aryl sulfone and palitaxel.

Note that the essence of this invention is the treatment of cancer. More particularly the claims herein set forth a method of lowering the incidence of side effects of known anti-neoplastic agents in a patient by employing a "cytoprotective agent." The *Kerkhoven* rejection is based on the employment of two separate actives known to be useful in treating the same population (i.e., cancer patients) recited in the claims herein. Therefore the rejection under *Kerkhoven* is indeed pertinent.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant finally argues that the cited prior art does not inherently disclose the protection of animals from the cytotoxic effects of anti-neoplastic agents by administering unsaturated aryl sulfones. Note that when aryl sulfone is administered to a patient (like in Reddy), along with an anti-neoplastic agent (as suggested by Griggs) the aryl sulfone compound will possess all of its qualities. One cannot separate a compound from its properties. Therefore the inherent qualities

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of the aryl sulfone compound, cytoprotective (as to normal cells) and cytotoxic (as to the tumor cells), will necessarily be present.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mojdeh Bahar whose telephone number is (703) 305-1007. The examiner can normally be reached on (703) 305-1007 on Monday, Tuesday, Thursday and Friday from 8:30 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Mojdeh Bahar  
Patent Examiner  
October 31, 2002

  
SREENI PADMANABHAN  
PRIMARY EXAMINER 11/3/02